

10/509513

DT04 Rec'd PCT/PTO 28 SEP 2004

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## CLAIMS

1. A method of treating a solid tumour in a subject, the method comprising the following steps
  - 5 (i) delivering to the solid tumour a composition comprising an engineered ovine atadenovirus and a lipid; and
  - (ii) administering a prodrug to the subject,wherein the engineered ovine atadenovirus comprises a promoter and a gene encoding an enzyme which converts the prodrug to a cytotoxic metabolite, the gene  
10 being under the control of the promoter.
2. A method as claimed in claim 1 in which the promoter is selectively active in a specific tissue.
3. A method as claimed in claim 1 or claim 2 in which the solid tumour is prostate cancer.
- 15 4. A method as claimed in claim 2 or claim 3 in which the specific tissue is prostate tissue.
5. A method as claimed in any one of claims 1 to 4 in which the promoter is a prostate specific membrane antigen promoter.
6. A method as claimed in any one of claims 1 to 5 in which the promoter is a  
20 probasin promoter.
7. A method as claimed in any one of claims 1 to 6 in which the ovine atadenovirus further comprises a transcriptional enhancer element.
8. A method as claimed in claim 7 in which the transcriptional enhancer element is from the prostate specific membrane antigen gene.
- 25 9. A method as claimed in any one of claims 1 to 8 in which the enzyme and the prodrug are an enzyme/prodrug combination selected from the group consisting of thymidine kinase/ganciclovir, thymidine kinase/acyclovir, bacterial cytosine deaminase /5-fluorocytosine, human cytochrome P450/cyclophosphamide or ifosfamide, thymidine phosphorylase/5'-deoxy-5-fluorouridine, cytosine  
30 kinase/cytosine arabinoside, *E. coli* GPT/ 6-thioxanthine, *E. coli* nitroreductase/5(-aziridine-1-yl)-2,4-dinitrobenzamide, and bacterial purine nucleoside phosphorylase/6-methylpurine-2-deoxyriboside or fludarabine.

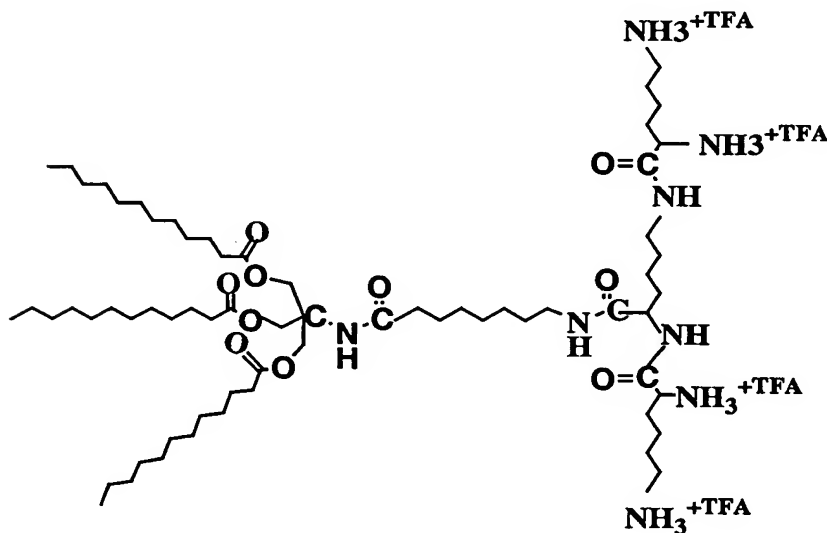
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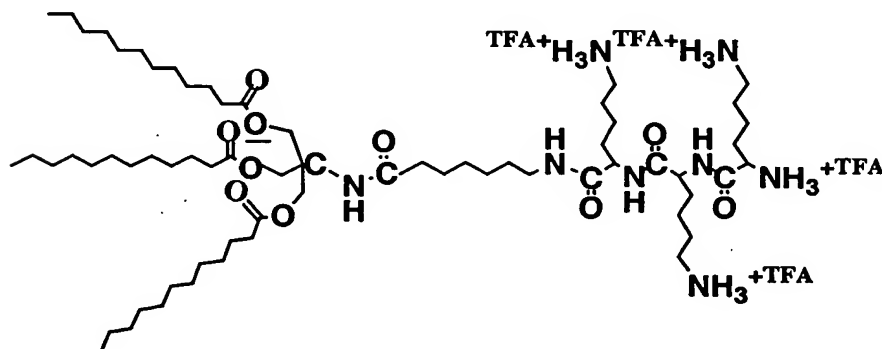
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10. A method as claimed in any one of claims 1 to 8 in which the enzyme is a purine nucleoside phosphorylase (PNP) and the prodrug is a purine prodrug which is converted by PNP to a toxic purine metabolite.
11. A method as claimed in claim 10 in which the prodrug is 6-methyl purine-2-deoxyriboside (6MPDR) or fludarabine.
12. A method as claimed in any one of claims 1 to 11 in which the lipid is a cationic lipid.
13. A method as claimed in any one of claims 1 to 12 in which the lipid is CSO87 having the formula :

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14. A method as claimed in any one of claims 1 to 12 which the lipid is CSO60 having the formula:



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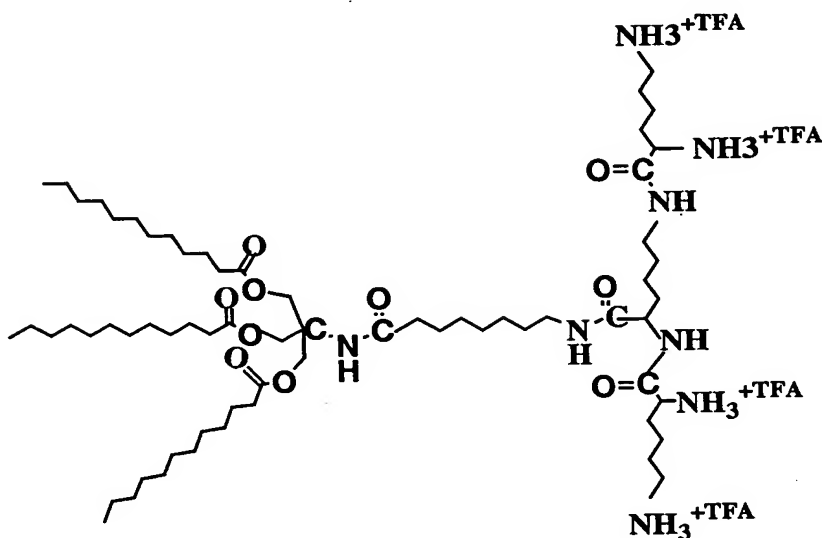
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15. A method as claimed in any one of claims 1 to 6 in which the engineered ovine atadenovirus is selected from the group consisting of OAdV220, OAdV223 and OAdV623.
16. A composition comprising
- 5 (i) an engineered ovine atadenovirus; and
- (ii) a lipid,
- wherein the engineered ovine atadenovirus comprises a promoter and a gene encoding an enzyme which converts a prodrug to a cytotoxic metabolite, the gene being under the control of the promoter.
- 10 17. A composition as claimed in claim 16 in which the promoter is selectively active in a specific tissue.
18. A composition as claimed in claim 16 or claim 17 in which the promoter is a prostate specific membrane antigen promoter.
19. A composition as claimed in any one of claims 16 to 18 in which the promoter is
- 15 a probasin promoter.
20. A composition as claimed in any one of claims 16 to 19 in which the ovine atadenovirus further comprises a transcriptional enhancer element.
21. A composition as claimed in claim 20 in which the transcriptional enhancer element is from the prostate specific membrane antigen gene.
- 20 22. A composition as claimed in any one of claims 16 to 21 in which the enzyme and the prodrug are an enzyme/prodrug combination selected from the group consisting of thymidine kinase/ganciclovir, thymidine kinase/acyclovir, bacterial cytosine deaminase/5-fluorocytosine, human cytochrome P450/cyclophosphamide or ifosfamide, thymidine phosphorylase/5'-deoxy-5-fluorouridine, cytosine
- 25 kinase/cytosine arabinoside, *E. coli* GPT/6-thioxanthine, *E. coli* nitroreductase/5(-aziridine-1-yl)-2,4-dinitrobenzamide, and bacterial purine nucleoside phosphorylase/6-methylpurine-2-deoxyribose or fludarabine.
23. A composition as claimed in any one of claims 16 to 21 in which the enzyme is a purine nucleoside phosphorylase (PNP) and the prodrug is a purine prodrug which
- 30 is converted by PNP to a toxic purine metabolite.
24. A composition as claimed in claim 23 in which the prodrug is 6-methyl purine-2-deoxyribose (6MPDR) or fludarabine.
25. A composition as claimed in any one of claims 16 to 24 in which the lipid is a cationic lipid.

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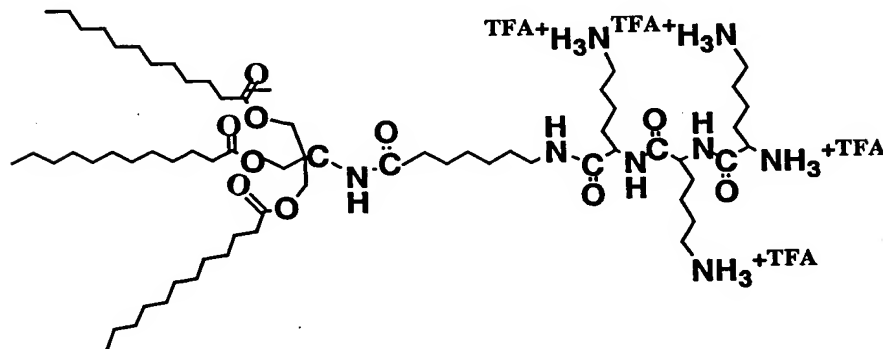
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26. A composition as claimed in any one of claims 16 to 25 in which the lipid is CSO87 having the formula :



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27. A composition as claimed in any one of claims 16 to 25 in which the lipid is CSO60 having the formula:



28. A composition as claimed in any one of claims 16 to 27 in which the engineered ovine atadenovirus is selected from the group consisting of OAdV220, OAdV223 and OAdV623.